

MEMORANDUM

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

TO : Director, National Heart and Lung Institute
Deputy Director, National Heart and Lung Institute
Director, Fogarty International Health Center

DATE: March 19, 1973

FROM : Dr. Lowell T. Harmison
Division of Technological Application
National Heart and Lung Institute

SUBJECT: Trip Report on Visit to the USSR Concerning Assisted Circulation and
Total Heart Replacement

1. Introduction.

The principal purpose of the visit was to determine the areas of work in assisted circulation, heart replacement and other areas of research and investigation of direct relevance to the artificial heart.

The visiting team consisted of Dr. Louis Rakita, Cardiologist, Case Western Reserve, Dr. Clarence Dennis and Dr. Lowell T. Harmison, National Heart and Lung Institute.

The program for the visit in the USSR was developed exclusively by the Russians with the principal coordinator being Dr. Valeriy I. Shumakov, Professor of Surgery, Research Institute of Clinical and Experimental Surgery in Moscow. A copy of the agenda for the period February 25 through March 4, 1973 is given in Attachment 1. It identifies the research institutes, clinics, principal investigators and time spent at these institutions plus other information concerning the visit. The scientific institutions and chief scientists visited were:

Research Institute of Clinical and Experimental Surgery, Moscow;
Professor B. V. Petrovsky

Research Institute of Medical Instrumentation, USSR Ministry of
Medical Industry; Dr. Michail Davidovich Pekarsky

Artificial Heart Laboratory of the Research Institute of Clinical
and Experimental Surgery; Professor Valeriy I. Shumakov

Bakulev Institute of Cardiovascular Surgery, Moscow;
Professor V. I. Burakovsky

Vishnevsky Institute of Surgery, Moscow; Professor A. A. Vishnevsky

Research Institute of Surgical Instruments and Devices, Moscow;
Dr. Rustam I. Utjamishev

Pulmonology Institute, Leningrad; Professor Georgy A. Rusanov
and Dr. Lydia P. Volkova

V. I. Kolesov's Clinic, Leningrad; Professors V. I. Kolesov and
E. V. Kolesov

In each of these institutes and clinics we met the director and the principal staff. In the following section, I will attempt to provide some detailed impressions and observations of the visit to Russia. It includes an overall summary and a discussion of each institute visited.

2. Summary.

Bearing in mind the limitations associated with: (1) the limited number of facilities visited, (2) the time available for discussion within each, and (3) the degree of exposure the Russians provided us with on each of the areas, I would summarize my observations as follows:

A. The research and development efforts in circulatory assist and total heart replacement are mundane. They are at least five years or more behind the efforts in this country. I saw no new avenues of research under study that have not been tried and rejected here or are under current investigation. I consider the development and testing efforts we saw very pedestrian in nature.

B. They are applying maximum effort to maintain awareness of U.S. efforts in both animal and clinical areas of study. This was demonstrated in terms of the types of devices which have been adapted for clinical use from commercial lines in the United States, the types of laboratory devices and techniques that we observed in both operative and postoperative procedures, the brochures and catalogs of American-type equipment, etc.

C. No areas of research probing the frontiers of either animal or clinical arenas were presented to us. The level of sophistication involved in the physical science and engineering research associated with the space program was not apparent in the biological and medical programs observed.

D. Their concept of evolving new devices and techniques, however, appeared very interesting. For example, it involves: (1) a medical research institute performing the basic research and establishing physiologic feasibility, (2) physical science/engineering institute developing prototypes for controlled laboratory and clinical evaluation, and (3) a subsequent institute for development of the large number of devices and their distribution to other cities and states within the Socialist Republic. However, no real evidence that the concept has worked was apparent outside of the development of the staple gun which is familiar to many. The multiple kidney dialysis unit, however, may be the first unit coming through the system.

E. The medical care system seemed to exhibit little lost motion in terms of patient flow from the outlying districts to the specialized clinics for study and treatment. Obviously, the quality of care delivered, its speed of application and overall effectiveness could not be gauged in the short time available. Nevertheless, their approach within each of the clinics visited seemed to be very direct and functional without a great deal of attention to peripheral matters.

F. Laboratory research seems to be well integrated with their clinical studies; however, the results of their laboratory investigations were never really made apparent to us in terms of biological data.

G. The emphasis appeared in most cases to be on clinical medicine rather than research. This applies even in the clearly identified research institutes.

H. The equipment, design of facilities, movement or flow of people, sterilization technique and general attention to detail seemed to leave many areas for improvement.

I. The work presented to us in our visits to Moscow and Leningrad was behind the state-of-the-art. Specifically, we saw no efforts toward noninvasive instrumentation and techniques for detection, diagnosing and monitoring disease, and no definitive research in hematology, hemodynamics, blood materials interface and other critical parameters essential to effective circulatory assist and total replacement research and development efforts.

J. The lack of open discussion on scientific questions concerning instruments, devices and techniques may have been due in large partly to the important patent question. At several points in discussions at different institutes, the proprietary question and patent activities were given as reasons for inability to discuss the area. In my view, this poses major questions and areas of difficulty which must be properly explored before effective communications and interactions can be developed for advancing this area of science. The concern stems not from the medical area but from the technologies involved because of their influence on items of commerce, defense, etc. There are three critical areas: (1) it limits scientific exchange between scientists (which we encountered); (2) it may significantly reduce incentives for participation on the part of the U.S. institutions in the performance of R&D efforts; and (3) it can have a major impact on the development, marketing and distribution of new medical instruments and devices throughout the United States. The reason

for concern in this matter is that the Russians may make minor modifications of U.S. technology and then secure or seek patent rights for such minor improvements in this country as well as in other Western countries. American and Western European companies might then have difficulty marketing products they have developed, even in their own country. It would appear that without effective exchange of ideas, this area will remain extremely unclear and therefore reduce incentives for participation by many of our contract and grantees in this kind of scientific exchange and have an impact as previously indicated on translating the fruits of research into tools of medical care and items of commerce.

I have the distinct feeling that more information existed in the relevant areas of CAD and total replacement than we were shown. It was also apparent that our visit was very carefully arranged by Dr. Shumakov; possibly it did not include other laboratories and facilities or efforts that may be in direct competition scientifically with his laboratory and associates. In my view, it is essential that the publications, questions to be answered, and other literature promised to us from the various laboratories be obtained and analyzed before any avenues of exchange can be effectively developed. A suggested second step beyond this might be a joint conference to present scientific material on relevant areas of circulatory assistance and total heart replacement for review and analysis, assuming that papers for the conference could be provided and reviewed by a joint editorial board prior to their acceptance for the meeting to insure some scientific meat in the papers to be presented. I would not advise additional onsite visits until these two steps have been accomplished.

3. Discussion of Each Institution Visited.

A. Research Institute of Clinical and Experimental Surgery, Moscow.

This research institute is under the direction of Professor B. V. Petrovsky. The first part of our visit to this institute was under the supervision of Dr. Shumakov, Professor of Surgery at the Institute and our principal host while in Russia. Dr. Shumakov gave us a tour of his clinical activities which included a visit to his dialysis unit, organ preservation lab and surgical facilities. The principal focus of Shumakov's activity in the clinical arena involves chronic uremic patients with treatment following either transplantation or dialysis. He has performed 183 kidney transplants and an additional two were performed during the day of our visit, one of which was performed by Dr. Shumakov. A few complications developed during the procedure; however, it was performed satisfactorily with total time requirement of about five hours. The procedure was relatively crude, e.g., the donor kidney had not been prepared until the recipient was ready to

receive it. Instrumentation was practically nonexistent in the operating room. According to our standards it would not be considered adequate. The dialysis unit consisted of a six-bed unit with central washing of the perfusate and individual controls for each of the patients being dialysed. The type of dialysing unit used is the Kiil unit. They have developed a solution for storing kidneys without perfusion for up to 32 hours. They would give us no details or even discuss the solution.

Animal Laboratory of the Institute: We visited the facilities that Shumakov uses in his work; they included both circulatory assist and total heart replacement experiments. The laboratory was adequately equipped with instrumentation, surgical facilities, mock circulatory loop units, biochemistry labs and other supporting chemistry labs to make it a complete research facility. Their experiments in the laboratory cover cardiac assistance through the heart-massage cup, the intra-aortic balloon, the series left assist heart, i.e., left atrium to ascending or descending aorta, various types of cannulation techniques for circulatory support, veno-venous and veno-arterio blood pumps of the pulsatile variety and partially implantable total heart devices, i.e., pumping chambers in thorax with the control unit and drive system external to the animal. Their work included both dog and calf species. A major percentage of their work has been in the area of circulatory assistance. The number of experiments performed by the laboratory exceeds 700, with probably over 500 being devoted to circulatory assist and the other experiments concerning various aspects of total circulation support and the artificial heart. The method of powering all of their units was pneumatic, with control for assist-type devices principally being derived from the QRS complex. When asked for specific information on method of control techniques for discrimination of arrhythmic signals and other parameters concerning synchronization and their effect on cardiac support, the questions went unanswered. For control of the total heart, they are developing an approach that utilizes stroke volume and aortic root stretch sensors and venous pressure for control. Again, we could elicit no scientific discussion on the system. We were told that it was still in the paper stage. In many cases, the answer was that the appropriate person(s) to provide the answers were not present, or I got a lengthy discussion that was a closed loop leading to no light on the question.

They showed us a variety of models of assist and total replacement hearts, most of which were copies of things that you could see in ASAIO proceedings from 1960 to 1965. The types of valving used in their pumps were ball, flap or disc valves. We did not see any valve research efforts. We were not shown any cardiovascular experiments or any real significant data from animal studies. We did see a pump functioning on the mock loop, but in a very typical display fashion. Most of the laboratory was idle during our visit. Possibly, this was arranged in order to have the people available for discussion; however, this objective was not apparently accomplished. In summary, I think the laboratory might be considered typical of several in the United States. It does have a large

number of personnel; without a specific headcount I would gather at least 75 to 80 people are involved in the animal research laboratories under Shumakov's direction in the area of assisted circulation and total heart replacement activities.

B. Research Institute of Medical Instrumentation, USSR Ministry of Medical Industry, Moscow.

The stated mission of this institute was for the production of the specialized medical instrument on a research scale for investigative purposes, not broad clinical uses. In essence, it was the pilot-type of research and development laboratory in support of medical research in the USSR. They presented us a broad outline of their activities in the heart and pulmonary area. The principal scientists making the presentations were Professors Kalantarov and Alexander Pistsov. The discussions were very circumspect and peripheral in nature. When asked for more scientific detail in most areas, it simply was not forthcoming. Again, the standard answer was people most familiar with the details of the research and development were not present or they were tied up in an experiment. The scientists at this institute collaborate closely with the medical schools and hospitals in the area and other cities to carry out their experiments on the prototype instrumentation. We did not see any research in progress at the institution. We did see much work in the area of mathematical modeling and fabrication of limited quantity-type units for both cardiovascular and pulmonary purposes. Their work included:

1. Pulsatile blood pump work with basic synchronization from the QRS complex with vacuum filling and without vacuum filling. The types of pumps are very similar to what has been under investigation for the previous eight or ten years in the U.S., basically nothing new. They gave us only limited performance parameters from a scientific point of view concerning the pumps and essentially no biological data on their performance. The materials of constructions included silicone, plexiglass, carbon and different types of urethanes.
2. Their work also included significant efforts on respirators and heart-lung machine development. However, all of the developments seen appeared to be within the state-of-the-art as we know it today.
3. They discussed the xenon injection techniques for evaluation of regional blood flow, including cerebral flow, but gave no data to back up their statements concerning accuracy and repeatability. This work appeared to be valuable but we will await review of requested reprints for any assessment.
4. They discussed a phonographic technique for assessing lung disease via application of an 80 Hz sound induction into the lung and making recordings with microphones to assess shifts in both frequency and amplitude, to obtain information concerning occlusions and other characteristics of the bronchi and smaller airway passages throughout inspiration and

expiration. Their research indicated that 80 Hz gave them more information than frequencies on either side. This is something which we should look into further in the lung area.

5. They are developing muscle stimulators utilizing very high frequency (2000 hertz and above) to avoid pain. Again, no specific data was presented to show the performance of these units.

6. They are developing an electronic sleep device to achieve deep sleep in the order of fifteen to thirty minutes. The device consists of approximately ten sensors positioned at different locations on the head, yielding electrical impulses of five millisecond duration at 100 cycles per second. No data were presented on this unit.

A number of other medical instruments were shown us. Literature on a variety of these units are in my file, should anyone desire to have more specific information. However, they are in the Russian language.

C. Bakulev Institute of Cardiovascular Surgery, USSR Academy of Medical Science, Moscow.

We received a general tour of the institute and discussion on each of its major principal areas - vascular disease, acquired heart disease and congenital heart disease. The institute had an area for performing assisted circulation; however, we received no details on its use other than a brief discussion regarding its application in terms of support for open heart procedures. They have also performed approximately forty coronary bypass procedures. However, when we asked about follow-up information and their feeling of effectiveness, we received very little discussion. In essence, arteriographic follow-up and careful analysis on the patients appeared to be lacking. The clinical facilities appeared to be adequate with sufficient instrumentation and equipment in the IC units for good care, including all of the necessary emergency equipment and supportive gas requirements. The intensive care units were filled with postoperative patients, not MI patients. This institute receives very few MI patients because we were told they were shunted to other facilities.

D. A. V. Visnevsky Institute of Surgery, USSR Academy of Medical Science, Moscow.

We had a general tour of the institute with discussions on most of its major activities. This included a film of open heart procedures, as performed in Russia, and their utilization of the heart-lung bypass machine; of a diagnostic program processed by the computer for handling problem cases from outlying medical institutions and regions around the country; and of electrical stimulators for bladder and intestine stimulation. The Vishnevsky

Institute has a much newer facility than those we generally visited on our tour. It was well equipped with six modern operating suites, which included TV monitoring of patients in both intensive and general care units and the incorporation of a nighttime technique for observation of the IC units involving the application of infrared light. The principal things of interest in this facility included a technique for measuring the depth of anesthesia by integrating the area under the EEG trace. I tried to explore this technique with them; however, it was unsuccessful because the people who know about it were apparently not there. I do feel this is a very interesting concept that possibly needs further study and evaluation here. The institution was using the xenon technique for regional and peripheral blood flow studies and studies of cardiac output and pulmonary blood flow. In each of the major laboratories in the facility, computer terminals exist for special calculations involving respiratory function and cardiac output and other parameters needed by the attending staff. An area concentrated on by the people who presented our tour included the RF stimulation technique for control of bladder and intestinal function. They have developed the RF technique for stimulation quite far, including proper placement of sensors in order to yield normal control of the bladder. Basically, this resulted in the placing of the negative electrodes in the neck of the bladder which afforded excellent control by the patient. The operating characteristics of their stimulator are current, approximately five microamps, at a voltage of ten to sixteen volts with a frequency of fifteen to twenty hertz. The stimulation threshold rises shortly after implantation; however, it stabilizes within the range indicated above within several weeks. The RF stimulation technique is also used for intestinal disorders, such as ulcers. They find that ulcers will heal within one month with application of the stimulation technique, versus one to two years without stimulation. The characteristics of the stimulation pulse are the same as for the bladder. We asked about the number of patients that had been treated, but it was unclear as to how large their data base was for making the assessment of more rapid healing.

This institute is, however, at the initial stage for application of the intra-aortic balloon. A few applications have been made; however, no significant data were available nor were they able to discuss the specifics of the unit. They also maintained an emergency cardiac unit involving the massage cup plus a variety of other emergency equipment, i.e., anesthesia, complete bypass units, respirators, defibrulators, etc., all in a room for immediate support of surgical and intensive care patients. We received no assessment of their performance and results.

E. Research Institute of Surgical Instruments and Devices, USSR
Ministry of Health, Moscow.

This institute is primarily involved in developing medical instruments for clinical application based on prototypes that

have proven satisfactory in early clinical trials. It also has the major responsibility for providing medical instruments and devices to all Socialist countries. Several devices made by this institution are:

1. The Vessel Stapler: This instrument has undergone continuous development from its inception. Now, in a single operation it can anastomose vessels of a diameter of 1.3 to 1.5 millimeters.
2. Dialysis Equipment: The units are now developed for multi-bed applications up to eight beds. The clinical dialyser is of the Kiil-type unit.
3. External Massage Unit: An external massage defibrillator unit, very similar to those in the United States.
4. Bypass Circulation Equipment: Extracorporeal circulation units with both roller- and pulsatile-type pumps for heart-lung applications have been fabricated. This laboratory also fabricates and provides devices to Dr. Shumakov's laboratory. Control units for the total heart replacement work are based on three parameters: (1) venous pressure, (2) stroke volume, and (3) some measure of distensibility of the aortic root. They would provide no details on this when questioned.
5. MI Detectors: A clinical unit for determination of MI based on the EKG; however, in a long series of questions we were unable to acquire any information about the system. They indicated that there would be some publications in the future which they would send to us. We asked them about the accuracy of the unit; they felt that 92 to 96 percent of the diagnosed cases of MI were picked up by this machine technique and that there existed only a two percent false positive and four to eight percent false negative indications. This all seemed a bit highly quantitative to us in the absence of no answers to our series of questions. I asked them if they have an operator's manual for the device since they have a number of units already in operation. They said, "No, it has not been assembled yet". The director, Rustam I. Utjamishev, indicated that this unit would be installed in the very near future in all cities with populations above 500,000.

The facilities within this institute seemed to be similar to those that we would find in various industrial laboratories throughout the United States. They had a well-equipped computer calculation center, electronics fabrication and test area, mechanical workshop area and well-equipped monitoring and test laboratories. They seemed to have a large activity in integrated circuits and other

smaller electronic components necessary for miniaturization and routine production of complex electronic systems. On their shelves, I noticed laboratory books and catalogs from such companies as Tectronics, Beckman and Hewlett-Packard.

They demonstrated to us an eight-patient dialysis unit with central automatic controls for a single operator that would permit monitoring each of the patients and the appropriate mixing and control of all parameters dealing with the eight beds, individually or collectively. The entire system, they pointed out, could be set up and functioning within three hours after arriving at an institution.

Although our visit was very interesting in terms of show and tell, we were really unable to determine any real basic scientific information. They would not give us information on their systems, indicating that the publications were yet to be put together.

F. Pulmonology Institute, USSR Ministry of Health, Leningrad.

The Pulmonology Institute coordinates all respiratory research and clinical studies in the USSR. The activities of the institute in Leningrad are directed to respiratory research on both the animal and clinical levels with an active interest in lung transplantation. It also has a significant team involved in circulatory assist and support efforts. In addition to these activities, it had the normal complement of backup laboratories and facilities that most large medical facilities have.

In the circulatory assist area, they have devoted most of their attention to short-term cardiovascular support approaches involving left-heart bypass and the intra-aortic balloon. None of their work has proceeded to the clinical level; they have carried out only limited animal studies with the intra-aortic balloon. They could not present any biological data concerning reduction in cardiac work, tissue damage, desired settings for synchronization and other parameters essential. This would appear to indicate that a significant base of research was not present. They have, however, tried the grandstand approach and have maintained an intra-aortic balloon in an animal for ten weeks without clotting, but they have only done one procedure in this time frame. When asked if they have established a protocol for patient selection and for application of the intra-aortic balloon, they indicated that none had been established. They felt that its principal use would be for the postsurgical patient. They are using carbon dioxide as their working gas with a polyvinyl type of balloon material coated with heparin. They indicated familiarity with the GBH approach; however, they did not elaborate when questioned about other techniques of surface coating or their results.

They have implanted a number of left-ventricular bypass pumps which have been used satisfactorily for periods of three weeks with up to sixty percent of cardiac output being taken by the pump and some lowering of left-ventricular pressure. They specific details on degree of reduction of cardiac work and left-ventricular pressure were not presented. When asked if they were considering cardiac models involving deteriorated function, they indicated they have not given any thought to these types of studies in order to assess the degree of cardiac assistance and true benefit to be gained by the left-heart bypass pump. They have developed a wide variety of designs with different inflow/outflow characteristics, including different types of valves in the various lines.

The laboratory also has a very active program in cardiac pacemaker development and clinical application. They did not indicate to us the number of pacemakers implanted; however, the number must exceed several hundred based on the patients and the type of development problems that they have considered. The laboratory has also developed a variety of support equipment for their lung-transplantation work. We asked them to provide us some literature which they indicated was available on the various types of lung preservation devices used in both autotransplant and homotransplant work. The laboratory has developed and is using, on both the clinical and laboratory level, a variety of pulmonary function equipment. In several cases, though, it appears that they have simply developed a Russian version of American equipment. Their research work has been limited to invasive techniques of PO_2 and CO_2 monitoring. They indicated, however, that noninvasive techniques of monitoring were being developed in Novosibirsk.

In terms of other hospitals visited, the Pulmonology Institute seemed to be very well organized and carried forth various echelons of intensive care treatment down to the general ward.

G. V. I. Kolesov Clinic - First Leningrad Medical Institute, Leningrad.

Professors V. I. Kolesov and E. V. Kolesov gave us a tour of the hospital facility. The principal emphasis of the institute is on coronary surgery and vascular surgery. Professor V. I. Kolesov initiated the internal-mammary to coronary-artery surgery successfully in 1964. They indicated that they see approximately eighty percent of coronary-artery disease involving the right and left vessel and only approximately twenty percent involving the circumflex. They perform their procedures without bypass circulation except for procedures involving the circumflex. This is similar to several facilities in the United States. Based on the expertise that they have developed in using the stapler, they feel the end-to-end anastomosis is much better than end-to-

side technique. They routinely make end-to-end anastomosis on diameters of approximately 1.3 millimeters. They have performed roughly a hundred coronary bypass procedures. Obviously, they felt very strongly about the procedure. When asked about follow-up studies on these patients, we found that only fifteen percent had been restudied and out of the fifteen percent, ten percent had been bad in terms of occlusion and five percent had remained patent. After finding out this information, I was not sure whether they were on firm ground concerning their strong interest in coronary bypass surgery; however, they indicated that they only do the follow-up on the severe patients because most will not permit effective restudy. I think the question still remains: is the patient alive because of the procedure, or would he be alive and in the same state without the procedure?

The laboratory has developed a rather elaborate EKG system for assessment of MI. They have a locus of points involving the 111 leads from which they feel they can determine, with approximately ninety-four percent accuracy, the state of the myocardial infarcts. They, however, admit limitations regarding posterior-wall infarcts. They have not developed nor or they applying vectoscadiography. In general, this institute seemed to be primarily devoted to coronary surgery with much less attention to other areas of cardiac and vascular surgery. Their facilities were on a par with other Russian facilities. They seemed to have a greater awareness of cardiac and cardiovascular surgery in the United States than other laboratories visited.

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Attachment